Refractory Adult Onset Still's disease successfully treated with Anakinra
Fátima Godinho, Maria José Santos, and José Canas da Silva

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Refractory Adult Onset Still’s disease successfully treated with Anakinra

Letter for the editor

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Pro-inflammatory cytokines like TNF-alpha, IL-6, IL-18 and IL-1 have been implicated in the pathogenesis of several chronic rheumatic inflammatory diseases including juvenile idiopathic arthritis and adult onset Still’s disease (AOSD)¹⁻⁵. The treatment of these diseases includes non-steroidal anti-inflammatory drugs (NSAIDs), systemic corticosteroids and in resistant cases, methotrexate (MTX), cyclophosphamide, sulfasalazine (SSZ) and cyclosporine A (CyA)⁶⁻⁸ have been used. Over the past years, several cases of successful treatment with infliximab and etanercept in AOSD, refractory to conventional therapy, have been published⁸⁻⁹.

We wish to report a very favourable response to Anakinra in a patient unresponsive to several DMARDs and TNFα blockers, requiring chronic high doses of steroids. The patient is a 32-year-old woman diagnosed, at the age 18, with AOSD, defined by the criteria of Yamaguchi et al.¹⁰. She was treated with NSAIDs, systemic steroids and several DMARDs (MTX, SSZ and CyA) over a period of 10 years, however, she had sustained disease with frequent flares requiring high doses of steroids (up to 1 mg/kg/day).

At the age of 28, she was referred to our rheumatology unit with persistent fever, arthritis, anaemia, leukocytosis and elevated serum levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and ferritin despite treatment with prednisolone 30 mg/day, naproxen 1g/day and MTX 20 mg/week. At examination she had six tender and six swollen joints and reduced range of motion of the neck, wrists and hips. Screening tests for infection were negative. She was treated with intravenous immunoglobuline (2 g/Kg), prednisolone and MTX was increased up to 25 mg/week subcutaneously (SC), and only showed a partial response. At two months follow-up the patient reported...
difficulty in walking with increased hip pain. Pelvic x-ray revealed bilateral asseptic necrosis of the femoral heads and she was admitted for total bilateral hip arthroplasty. In October 2000, infliximab was added to her treatment, initially at a dose of 3 mg/kg and increased to 5 mg/kg. Six months later she continued to have fever, arthritis (19 tender and 2 swollen joints) and elevated ESR (117 mm/h) and infliximab was discontinued. She was switched to Etanercept, 25 mg SC, twice a week for 54 weeks, with very little clinical response. Throughout this period she continued to have intermittent fever, arthritis and elevated serologic inflammatory markers. In October 2002 it was decided to attempt Anakinra 100 mg/day SC in addition to MTX 25 mg/week SC, prednisolone 20 mg/day and naproxen. An impressive response, both in systemic features and joint disease occurred over the first weeks of treatment and acute phase reactants returned to normal. Steroids could be reduced and discontinued. Anakinra was well tolerated and no adverse effects were observed. After 18 months of follow-up the patient remains in full clinical remission, without steroids or NSAIDs (Table I).

<table>
<thead>
<tr>
<th>INFLIXIMAB</th>
<th>ETANERCEPT</th>
<th>ANAKINRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jun 00</td>
<td>Oct 00</td>
<td>Jun 01</td>
</tr>
<tr>
<td>Aug 01</td>
<td>Sept 02</td>
<td>Oct 02</td>
</tr>
<tr>
<td>Mar 04</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Hemoglobin (mg/dl)</th>
<th>8.9</th>
<th>8.8</th>
<th>9.4</th>
<th>8.7</th>
<th>9.2</th>
<th>9.2</th>
<th>12.4</th>
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<tr>
<td>Leukocytes (x10⁹/L)</td>
<td>18.300</td>
<td>26.300</td>
<td>26.020</td>
<td>17.100</td>
<td>23.600</td>
<td>23.600</td>
<td>8.100</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>112</td>
<td>120</td>
<td>117</td>
<td>120</td>
<td>107</td>
<td>112</td>
<td>13</td>
</tr>
<tr>
<td>Platelets (x10⁹/L)</td>
<td>591</td>
<td>777</td>
<td>703</td>
<td>689</td>
<td>748</td>
<td>748</td>
<td>387</td>
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<td>yes</td>
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<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>No</td>
</tr>
<tr>
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<td>yes</td>
<td>yes</td>
<td>yes</td>
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<td>No</td>
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<td>yes</td>
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<td>No</td>
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<tr>
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<td>30</td>
<td>15</td>
<td>20</td>
<td>20</td>
<td>0</td>
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</table>

Table I: Clinical evolution of the patient

This is, to our knowledge, the first reported case of successful treatment of AOSD with Anakinra. Although TNFα antagonists have revolutionized the treatment of refractory AOSD, there are patients who do not respond to this treatment. The dramatic response to Anakinra in this case of AOSD refractory to conventional therapies and to anti-TNF-α
blockers, suggests that the inhibition of IL-1 can be an important therapeutic target in some patients.

References:


